REMARKS

Favorable reconsideration of this application is requested in view of the amendments above and the remarks/arguments which follow.

Disposition of the Claims

Claims 37-44 and 46-50 are pending in this application. Claims 19, 20, and 45 have been canceled. The subject matter of claim 45 has been incorporated in claim 37.

Rejections Under 35 U.S.C. §112

Claims 37-50 were rejected under 35 U.S.C. § 112, second paragraph, as being incomplete for omitting essential elements. Claim 45 has been canceled. Accordingly, rejection of this claim is moot. The remaining claims have been amended as set forth above to include the essential elements. Withdrawal of this rejection is respectfully requested.

Rejections Under 35 U.S.C. §103

I. Claims 19, 20, 37-44, 46, 48, 49, and 50 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Pozzi et al. (U.S. Pat. No. 5,629,017) in view of Benton et al. (U.S. Pat. No. 4,876,094), Oshlack et al. (U.S. Pat. 5,356,467), and Cortese et al. (U.S. Pat. No. 4,327,725). Claims 19-20 have been canceled. Accordingly, rejection of these claims is moot. Reconsideration of the rejection of claims 37-44, 46, 48, and 50 is respectfully requested.

Pozzi et al. teach a dual-coated dosage form that includes a core containing drug, a hydrophobic subcoat formed on the core, and an enteric overcoat formed on the hydrophobic subcoat. It is well known in the pharmaceutical art that enteric coating on oral dosage forms readily dissolve when such dosage forms transit from the low pH environment of the stomach to the higher pH environment of the gastrointestinal tract. This rapid dissolution of the enteric overcoat teaches away from the exterior membrane recited in claim 37, which remains at least partially undissolved throughout the functional life of the dosage form, even in the pH of 7-8 environment of the colon, becoming more permeable to lipids in later hours as the peptide within the exterior membrane gradually is enzymatic ally degraded.

The hydrophobic subcoat of the Pozzi et al. dosage form is based on waxes. Such waxes have low molecular weights and as such are known to be brittle solids that break up easily when mechanically insulted, which then would be expected to mechanically fail when subjected to the churning and peristalsis of the gastrointestinal tract. The selection of waxes by Pozzi et al. leads away from the use of a tough, hydrophobic high molecular weight polymer, i.e., poly(ethyl cellulose), as the base polymer of the interior membrane recited in claim 37. Ethyl cellulose is a tough polymer, so tough in fact that it is used as a protective lacquer coating for bowling pins. It is unobvious in view of Pozzi et al. that such a tough polymer would be selected as a major component of a membrane to disintegrate within the gastrointestinal tract.

Benton et al. teach a dual-coated dosage form that includes a matrix core, a hydrophobic subcoat formed on the matrix core, and a hydrophilic overcoat formed on the hydrophobic subcoat. The hydrophobic subcoat is based on fats that melt near body temperature. This is in contrast to the invention recited in claim 37, wherein the interior membrane includes poly(ethyl cellulose) polymer as a base polymer. While the hydrophilic overcoat taught by Benton et al. can include zein, the function of the overcoat is merely to prevent agglomeration of the drug particles while they are dispersed in an aqueous sugar syrup prior to oral administration. The hydrophilic overcoat is not formulated and configured to delay disintegration of the hydrophobic subcoat.

In use, neither the hydrophobic subcoat nor the hydrophilic overcoat taught by Benton et al. provides any rate control element to drug release other than simple enteric properties. Once administered to a patient, the bilayer coating rapidly dissolves when emptied from the stomach to the intestine. Any rate control of drug release at that point is due solely to the release of drug from the matrix core (col. 7, lines 64-67), not the properties of the coating. There is no membrane control whatsoever. In contrast, the bilayer membrane recited in claim 37 controls drug release rate down for many hours while the dosage form is transiting the gastrointestinal tract. Further, Benton et al. do not anticipate lipid or sorption as the source of degradation of the bilayer coating as none of their in vitro tests include the effects of lipids.

Oshlack et al. teach zein coating compositions where zein is the major component and continuous phase of the coating. Oshlack et al. disclose that pore-formers can be blended into the zein, which pore formers in an aqueous environment dissolve and leave behind channels in

the major phase (col. 8, lines 59-61). He further discloses that semipermeable polymers such as cellulose acylates can be blended into zein as a pore former (col. 9, lines 20-24). This teaches away from the present invention where semipermeable polymer is disclosed as a major and continuous phase of the coating, present at a level of 35 to 70 wt%, and zein as the minor and discontinuous phase of the coating, present at a level of only 20 to 35%.

If Pozzi et al., Benton et al., and Oshlack et al. are combined, the result would be a dosage form having a subcoat based on fats that melt near body temperature or low molecular weight waxes and an overcoat that is either an enteric coating or that includes zein as a major and continuous phase and a semipermeable polymer as a pore former. This combination does not anticipate or make obvious claim 37 as amended. Further, Cortese et al. do not overcome the deficiencies in the Pozzi et al., Benton et al., and Oshlack et al. references nor do they anticipate or make obvious the use of swellable hydrogels present within the tablet core as a source of polymeric swelling pressure to promote rupture of external membranes after the dose of drug has been delivered. In the claimed invention, the internal swelling pressure of the swollen hydrogel after the drug layer has been dispensed is used unexpectedly in concert with the self-destructive membrane having enzymatic attack and lipid sorption mechanisms to achieved timed degradation of the exterior membrane.

From the foregoing, it is clear that claim 37, as amended, is not obvious over the combination of Pozzi et al., Benton et al., Oshlack et al., and Cortese et al. Withdrawal of the rejection of claim 37 over the combination of these references is respectfully requested. Claims 38-44, 46, and 48-50, being dependent on claim 37, are likewise patentable in view of the foregoing arguments.

II. Claims 19, 20, and 37-50 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Zeitoun et al. (U.S. Pat. 4,432,966) over Seminoff et al. (U.S. Pat. No. 5,126,146), Staniforth (U.S. Pat. 5,504,614) and Oshlack et al. (U.S. Pat. 5,356,467). Claims 19, 20, and 45 have been canceled. Accordingly, rejection of claims 19, 20, and 45 is moot. Reconsideration of the rejection of claims 37-44 and 46-50 is respectfully requested.

Zeitoun et al. teach a dosage form having an enteric overcoat that rapidly dissolves when passing from the gastric to the intestinal pH. This teaches away from the exterior membrane recited in claims 37-44 and 46-50, which remain on the exterior of the dosage form for prolonged periods of time during the functional life of the dosage form, becoming more permeable to lipids in later hours as the peptide polymer within the exterior membrane is gradually enzymatic ally degraded.

With respect to Seminoff et al., the Examiner correctly points out that the claimed invention relies on the use of pore formers, e.g., ethyl cellulose, in the subcoat layer, but this is just one aspect of the invention. The use of the semipermeable material in the exterior membrane is also important to achieving the desired bilayer membrane behavior. However, Seminoff et al. teach away from the claimed invention by indicating that the coating around the tablet core must not be covered on the inner or outer surface by a semipermeable layer (col. 2, lines 34-37).

Staniforth teaches a diffusional system while the claimed invention is an osmotic system. The ethyl cellulose wall disclosed by Staniforth serves as an impermeable coating that localizes the entry of water into the device through the large delivery port. This construction teaches away from the invention recited in claim 50 where rate control is governed by the osmotic imbibition of water into the delivery system through the bilayer membrane coating, forcing the drug formulation to be pumped from the exit. In Staniforth, water both enters and leaves the delivery device through the large delivery port. This is contrary to the invention recited in claim 50 where water enters the system through the membrane and leaves the system from the exit.

From the foregoing, claims 37-44 and 46-50 are not rendered obvious in view of the combination of Zeintoun et al., Seminoff et al., and Stanforth. The Oshlack et al. reference has already been discussed above and fails to overcome the deficiencies in the Zeintoun et al., Seminoff et al., and Stanforth references. Withdrawal of the rejection of claims 37-44 and 46-50 is respectfully requested.

Conclusion

The rejected claims have been amended and/or shown to be allowable over the prior art. Applicants believe that this paper is fully responsive to each and every ground of rejection cited by the Examiner in the Office Action dated July 2, 2003, and respectfully request that a timely Notice of Allowance be issued in this case.

Please apply any charges not covered or any credits to Deposit Account 10-0750.

Respectfully submitted,

Date: 1/2/2004

Adenike Adewuya

Adenike A. Adewuya
Registration No. 42,254
Tel.: (281) 477-3450